UNIVERSITY OF LINCOLN

How effective are Z-drug hypnotics for treatment of adult insomnia? Meta-analysis of data submitted to the Food and Drug Administration

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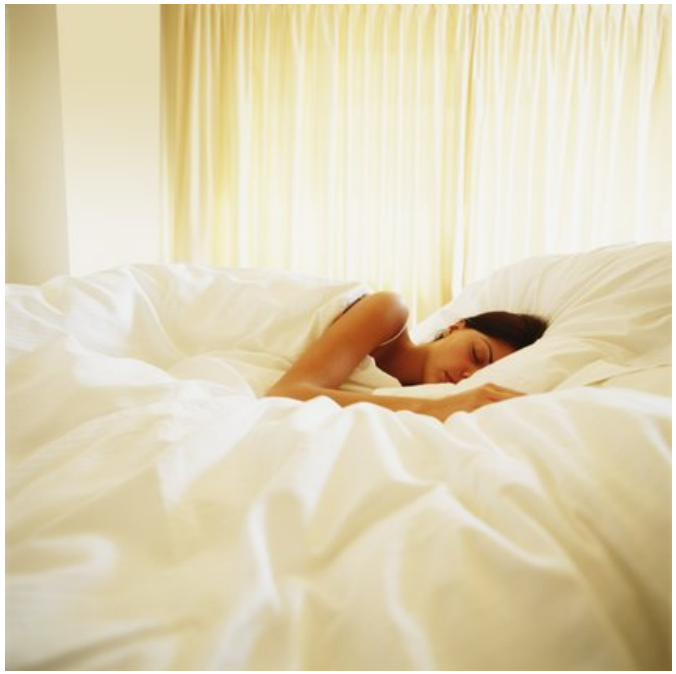
Insomnia

- Common
- Quality of life, work
- Treatment



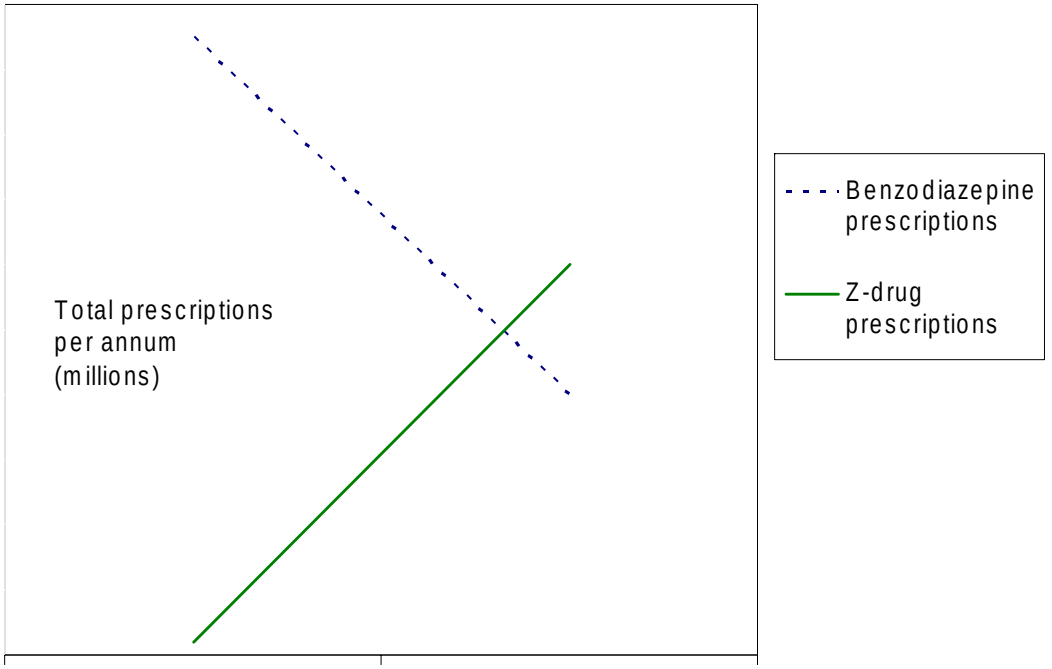
Dyas JV et al. Patients' and clinicians' experiences of consultations in primary care for sleep problems and insomnia: a focus group study. BJGP 2010; 60: 329 -333.

Practitioner beliefs and behaviours

	Insomnia preference ranking (1, highest-9, lowest)
Benzodiazepine	**5**
'Z' drug	**2**
Brief psychotherapy	-
Anxiety advice sheets	-
GP verbal advice	**1**
Sleep hygiene advice sheets	**4**
Sleep restriction	7
Sedative antihistamines	6
Phenothiazines	9
Sedative antidepressant	**3**
Non-sedative antidepressant	8
Referral to counsellor	-
Referral to CPN	-
Other referral	-

Siriwardena AN et al. General practitioners' preferences for managing insomnia and opportunities for reducing hypnotic prescribing. J Eval Clin Pract 2010;16: 731–737.

Drugs for sleep

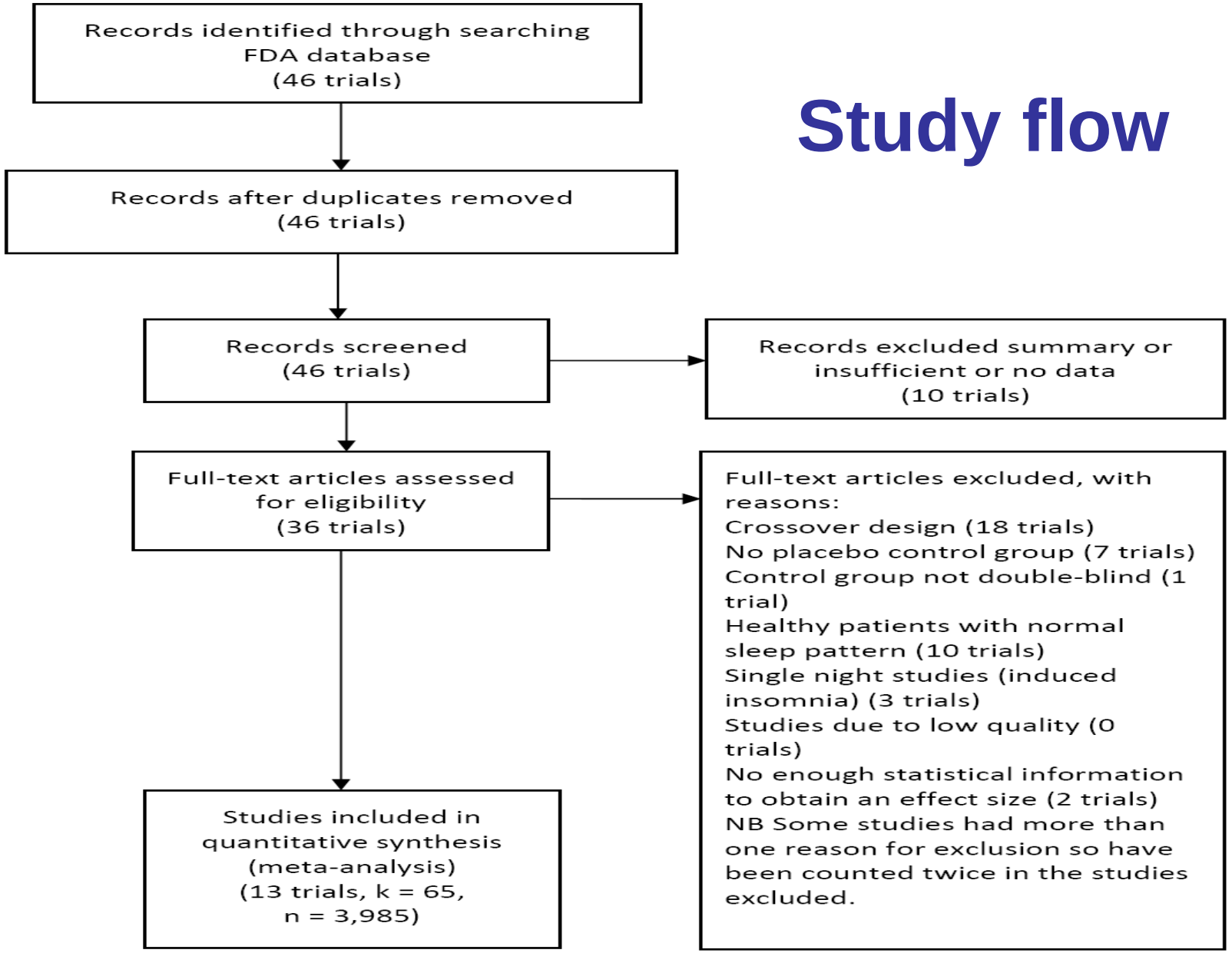


Siriwardena AN et al. Magic bullets for insomnia? Patients' use and experience of newer (z drugs) versus older benzodiazepine) hypnotics for sleep problems in primary care. *Br J Gen Pract* 2008; **58**: 417-22

Food and Drugs Administration

- Data on approved drugs
- Data on all currently approved (non-benzodiazepine) Z-drugs: eszopiclone, zaleplon and zolpidem from the FDA website
- Quality rating
- PRISMA guidelines

Study flow


Records identified through searching FDA database (46 trials)
Records after duplicates removed (46 trials)
Records screened (46 trials)
Records excluded summary or insufficient or no data (10 trials)
Full-text articles assessed for eligibility (36 trials)
Full-text articles excluded, with reasons:
Crossover design (18 trials)
No placebo control group (7 trials)
Control group not double-blind (1 trial)
Healthy patients with normal sleep pattern (10 trials)
Single night studies (induced insomnia) (3 trials)
Studies due to low quality (0 trials)
No enough statistical information to obtain an effect size (2 trials)
NB Some studies had more than one reason for exclusion so have been counted twice in the studies excluded.
Studies included in quantitative synthesis (meta-analysis) (13 trials, k = 65, n = 3,985)

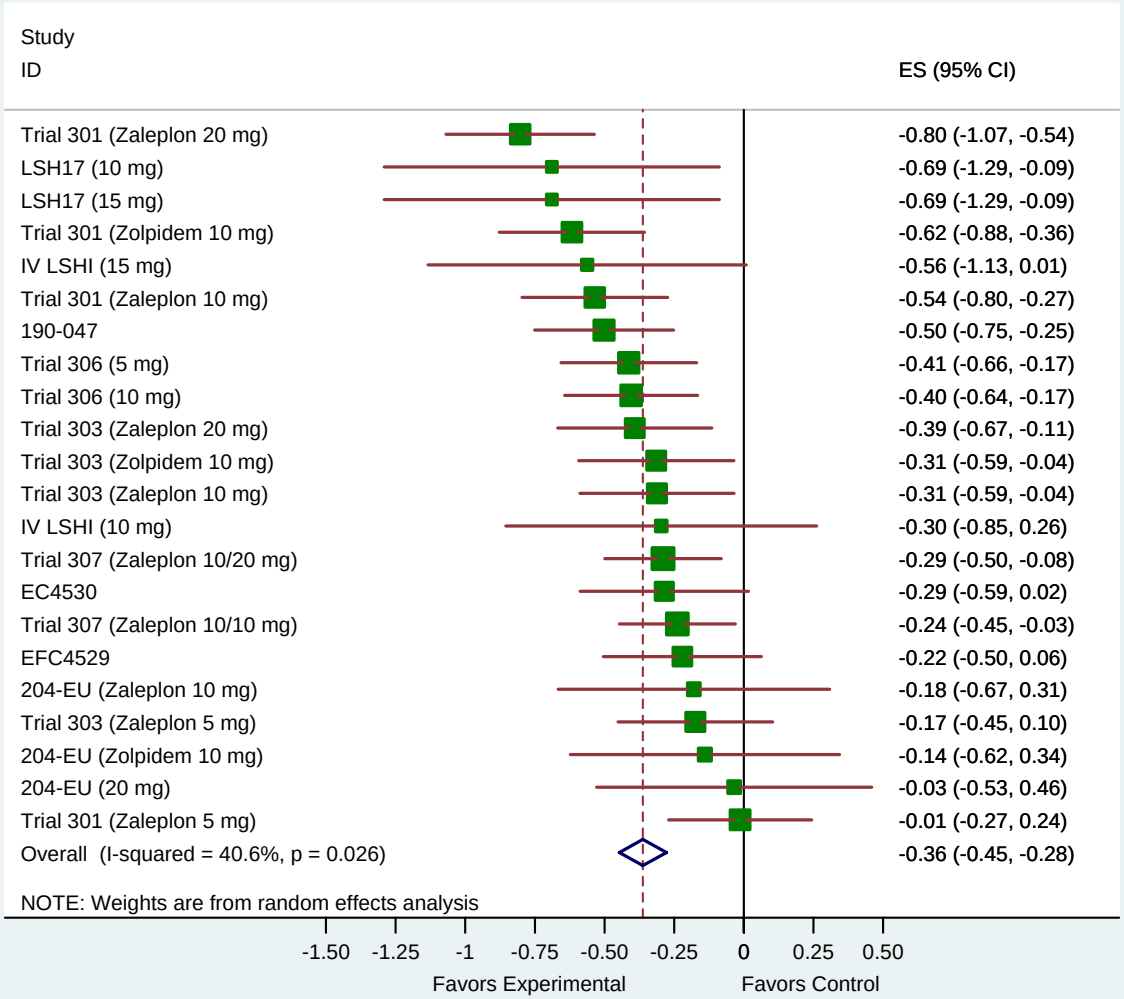
Results

- 13 studies
- 65 drug-placebo comparisons (k) by outcome, drug and dosage
- 3985 subjects
- Different countries, treatment lengths, year of study

Sleep latency: weighted standardized mean differences

Primary outcomes		Within Group Weighted mean *d*+ (95% *CI*)		Between Group Weighted mean *d*+ (95% *CI*)
	k	Experimental	Control	Experimental vs. Control
Sleep latency PSG	16	-0.93 (-1.32 to -0.54)	-0.39 (-0.54 to -0.23)	-0.36 (-0.57 to -0.16)
Sleep latency subjective	4	-0.67 (-1.30 to -0.034)	-0.33 (-0.63 to -0.033)	-0.33 (-0.62 to -0.041)

Sleep latency (PSG)



Experimental versus control group effect sizes of sleep latency PSG ordered by magnitude

Sleep latency: weighted raw mean differences

Primary outcomes		**Within Group Weighted mean *d*+ (95% *CI*)**		**Between Group Weighted mean *d*+ (95% *CI*)**
	k	**Experimental**	**Control**	**Experimental vs. Control**
Sleep latency PSG	14	**-42 (-60.0 to -23.0)**	**-20 (-28.0 to -11.0)**	**-22.0 (-33.0 to -11.0)**
Sleep latency subjective	2	**-25 (-30.1 to -19.9)**	**-19.4 (-26.6 to -12.2)**	**-6.9 (-26.0 to + 12.4)**

Homogeneity of effect sizes

Primary outcomes		Homogeneity of effect sizes I2 (95% CI)		
	k	Experimental	Control	Experimental vs. Control
Sleep latency PSG	16	89 (83.58 to 92.47)	0 (0 to 77.60)	41 (1.18 to 64.30)
Sleep latency subjective	4	0 (0 to 49.26)	0 (0 to 66.15)	83 (70.98 to 90.05)

Moderator analysis

Moderator variable	d_+(95% CI for d_+)	β
Sleep latency PSG		
Dosage (*k* = 22)		-0.22*
1 mgs	-0.24(-0.38 to -0.11)	
20 mgs	-0.50 (-0.64 to -0.35)	
Sleep latency subjective		
Year of data collection (*k* = 9)		0.63***
1988	-0.88 (-1.19 to -0.58)	
2004	-0.032 (-0.16 to 0.098)	
Age (*k* = 9)		0.89***
38 years	-0.65 (-0.82 to -0.48)	
72 years	0.31 (0.13 to 0.50)	
Percentage of women (*k* = 9)		-0.40**
55.9 %	0.0050 (-0.17 to 0.18)	
67.5 %	-0.67 (-0.99 to -0.34)	
Dosage (*k* = 11)		-0.70***
1 mgs	0.13 (-037 to 0.30)	
20 mgs	-1.006 (-1.31 to -0.70)	

Conclusions

- Z-drugs have limited benefit
- Small reductions in subjective and PSG sleep latency especially with larger dosages
- No improvement in other sleep measures compared to placebo.
- Placebo effects were moderate for sleep latency.
- Hypnotics are more effective in women, younger patients, larger drugs doses and older studies

Project partners

- University of Lincoln: Community and Health Research Group
- University of Connecticut: Tania Huedo-Medina
- Harvard University: Irving Kirsch

REST

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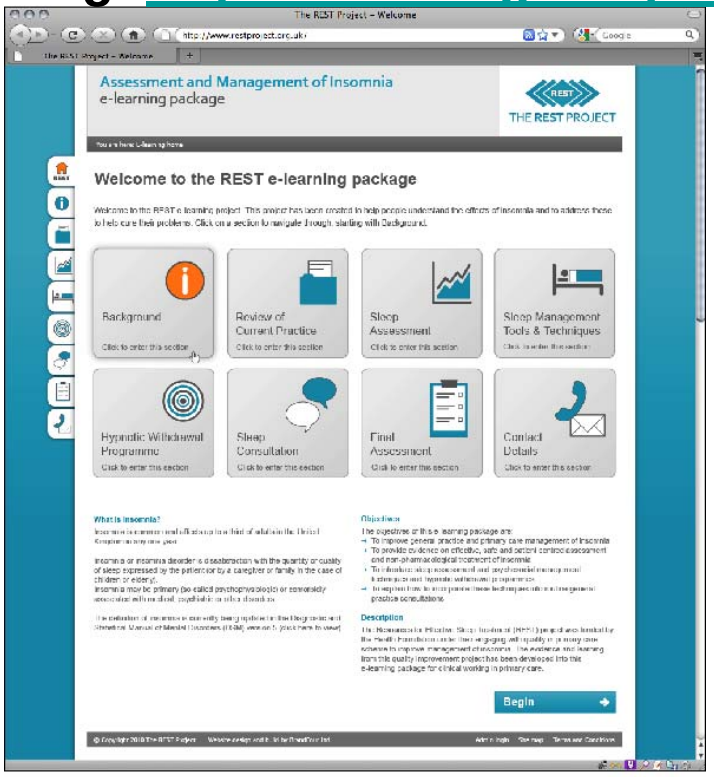

Thank you